Remarks

Claims 23-26 and 31-37 are pending in the subject application. By this Amendment, Applicants have amended claims 23, 31, 33, 34 and 36 and added new claim 38. Support for the amendments and new claim can be found throughout the subject specification and in the claims as originally filed (see, for example paragraph 168 of the published application). Entry and consideration of the amendments presented herein is respectfully requested. Accordingly, claims 23-26 and 31-38 are currently before the Examiner. Favorable consideration of the pending claims is respectfully requested.

Applicants gratefully acknowledge the Examiner's withdrawal of the objection to claim 23 and the rejections under 35 U.S.C. § 112, first paragraph, and 35 U.S.C. § 103(a) (over Fox *et al.*).

Applicants gratefully acknowledge the Examiner's indication that claims 23-26 and 36-37 are allowed.

Claims 31-35 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully assert that there is adequate written description in the subject specification to convey to the ordinarily skilled artisan that they had possession of the claimed invention. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Regarding the issue raised with respect to the recitation of the cations identified in claims 31 and 33, Applicants submit that the amendment of these claims to depend from allowable claim 23 has rendered this issue moot. Accordingly, reconsideration and withdrawal of this aspect of the invention is respectfully requested.

With respect to the issue raised regarding the recitation of the term "antigen" in claim 35, Applicants respectfully disagree with the Examiner's assessment and traverse the rejection of record. Applicants note, at the outset, that the Office Action argues that "[f]unctional language, at the point of novelty, as herein employed by Applicants, is admonished in *University of California v. Eli Lilly and Co.* ...". Applicants respectfully submit that this assessment is in error. In cases such as *Fiers* and *University of California v. Eli Lilly and Co.*, the patent specifications at issue did not identify the

sequence (structure) of any embodiment of DNA claimed thercin. *See Eli Lilly,* 119 F.3d at 1567-68 (affirming a judgment that the claim requiring cDNA encoding human insulin was invalid for failing to provide an adequate written description where the specification described the human insulin A and B chain amino acid sequences encoded by the cDNA, but did not provide the nucleotide sequence for the cDNA itself); *Fiers,* 984 F.2d at 1167-68, 1170-71 (finding the written description insuffieient where the patent claimed purified DNA encoding human fibroblast interferon-beta polypeptide, but the specification only disclosed a bare reference to DNA and suggested a process to sequence it). In contrast, the instant specification is directed to novel chemical compounds that stimulate γδ T cells, for which adequate written description exists within the as-filed specification. The point of novelty in this matter does not relate to the antigens recited within the claims. Under both the *University of California* and *Fiers* analysis, the as-filed specification is sufficient to describe the claimed compounds.

Applicants also respectfully refer the Examiner to *Capon v. Eshhar*, 76 USPQ2d 1078, 1085 (Fed. Cir. 2005) where it is noted that there is no "per se rule that the information must be determined afresh" when the nucleotide information is included in the prior art. Moreover, it is emphasized that a "re-description of what was already known..." Id at 1084, has never been required, in contrast to oft-cited cases such as *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) where the cDNA for human insulin had never been characterized. In this case, numerous examples of antigens were known in the art well before the earliest effective filing date of this application. For example, the textbook *Immunology* (published in 1992 by Janis Kuby) contains an entire chapter dedicated to antigens. For example, at page 73 it is taught that: "Antigens are substances able to induce a specific immune response." A similar definition is found in *Immunology: An Illustrated Outline* by David Male (1986;l a copy of which is attached for the convenience of the Examiner). Accordingly, it is respectfully submitted that the as-filed specification provides adequate written description for the term "antigen" and reconsideration and withdrawal of the rejection is respectfully requested.

Claim 35 has been amended to recite a list of antigens, support for which is found in paragraph 0168, thus rendering this aspect of the rejection moot.

Claims 33-35 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for immunotherapy or stimulation of an immune response in a subject suffering from an infectious disease, does not reasonably provide enablement for immunotherapy or stimulation of an immune response in a subject suffering from a tumor, solid tumor, or an autoimmune disease or an allergic disease. Applicants respectfully assert that the claims as filed are enabled.

The Examiner asserts that there is no specific data within the as-filed specification that enables the claimed invention. In essence, the Office Action appears to argue that experimental evidence or working examples are required within the as-filed specification in order for the enablement aspect of 35 U.S.C. § 112, first paragraph to be satisfied in this matter. Applicants respectfully submit that compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed (see M.P.E.P. §2164.02). Indeed, the Federal Circuit has held that "The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 U.S.P.Q. 2d 1302, 1304 (Fed. Cir. 1987) (quoting *In re Chilowsky*, 229 F.2d 457, 461, 108 U.S.P.Q. 321, 325 (C.C.P.A. 1956)). The Federal Circuit's predecessor court also indicated that the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 U.S.P.Q. 642, 645 (C.C.P.A. 1970).

Applicants respectfully traverse this rejection and contend that the claimed invention has been enabled by the as-filed specification. The attention of the examiner is drawn to the fact that those skilled in the art generally recognize the benefit of treating tumors with γδ T-cells. For example, Kabelitz *et al.* (*Cancer Res.*, 2007, Vol. 67, pp. 5-8) discusses the status and perspectives of γδ T-cells in tumor immunology. As noted in that paper at page 7, column 1:

> **Tumor-infiltrating γδ T cells are tumor reactive.** γδ T cells have been consistently identified and isolated from TIL in various types of cancer, including colorectal, breast, prostate, ovarian, and renal cell carcinoma (4, 5, 9, 12, 14). γδ T cell lines and clones established from TIL recognize and kill not only the autologous tumor but generally also a broad range of related tumors, presumably due to the

recognition of shared ligands as described above. Importantly, the γδ T cells preferentially kill tumor cells and show low (if any) reactivity towards nontransformed cells, a feature that has raised great interest to explore their therapeutic potential (9, 12).

Tumor-reactive γδ T cells are stimulated by phosphoantigens and aminobisphosphonates. Synthetic phosphoantigens, such as bromohydrin pyrophosphate (Phosphostim) and aminobisphosphonates, are potent activators of Vδ2Vγ9 T cells. In the presence of interleukin-2 (IL-2), these ligands induce a rapid and exponential expansion of γδ T cells to large cell numbers for potential application in adoptive cell transfer (9). In vitro expanded Vδ2Vγ9 T cells maintain their antitumor activity in vivo upon adoptive transfer into immunodeficient mice transplanted with human tumor cells, indicating the feasibility of this approach in a preclinical model (17). Therefore, two strategies for the potential usage of γδ T cells in tumor immunotherapy are presently being envisaged i.e., the adoptive cell transfer of in vitro expanded γδ T cells and the in vivo therapeutic application of γδ - stimulating phosphoantigens or aminobisphosphonates together with low-dose IL-2 (Fig. 1B). Ongoing clinical phase I trials evaluate Phosphostim together with low-dose IL-2 in patients with renal cell carcinoma (18), and other types or cancer, including pancreatic adenocarcinoma and colon carcinoma, are under consideration. Trials with aminobisphosphonates plus IL-2 are also done in multiple myeloma (11).

Accordingly, it is respectfully submitted that the as-filed specification enables the claimed invention and reconsideration and withdrawal of the rejection is respectfully requested.

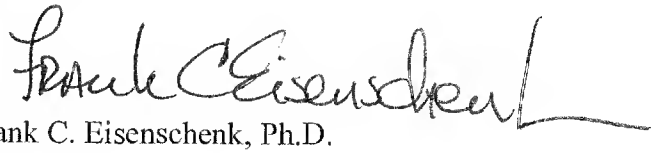
It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and amendments to the claims, Applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

Applicants invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,



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